Rejection of Claims 14-21 and 42 Under 35 U.S.C. § 112, 2nd ¶

Claim 14 is allegedly unclear for failing to articulate the connection between the method step and the preamble. Claim 14 has been amended to articulate the connection, thus obviating the rejection.

Claim 17 was rejected as the phrase "part of human wild-type p53 protein" was unclear as to its metes and bounds. This rejection is respectfully traversed.

Claim 17 recites a polypeptide. A polypeptide by definition does not include within its scope a single amino acid, as the Office Action speculated "a part" could include. A polypeptide is defined as many amino acids bonded together or an organic compound consisting of three or more amino acids. See www.ntri.tamuk.edu/cell/chapter3 and www.fleshandbones.com/genetics/mueller/glossary. Moreover, claim 17 incorporates all limitations of claim 14. Claim 14 requires that the compound (here a polypeptide) "is able to complex specifically with a p53-specific binding site." It is extremely unlikely that a single amino acid could have such ability. Thus claim 17 due to its terms and its functional limitation does not read on the use of a single amino acid and its metes and bounds are clear.

Claim 19 has been amended to delete the phrase "a portion of the monomer sequence" which was objectionable, thus mooting this ground. However, claim 19 was also rejected as unclear in the phrase "sequences adjacent to the monomer sequence in the human genome." The Patent and Trademark Office urges that the phrase could read on both a single nucleotide as well as the whole human genome. Claim 19 has been amended to recite that the compound "comprises an oligonucleotide or oligonucleotide containing nucleotide analogs wherein said oligonucleotide or oligonucleotide containing nucleotide analogs comprises at least one monomer ... as well as sequences adjacent..." An oligonucleotide is defined as a chain of literally, a few nucleic acids. See

www.fleshandbones.com/genetics/mueller/glossary. While an oligonucleotide could comprise at least one monomer plus just one nucleotide of adjacent sequence, it could not include the whole human genome due to the recitation of "an oligonucleotide." The recitation of an oligonucleotide is supported at page 16, line 8 and following.

Claim 20 is also said to be unclear because the phrase "more than one monomer" has no upper limit. The Patent and Trademark Office asserts that the claim could read on an infinite number of monomers. That reading, however, is untenable. The claim recites an "oligonucleotide" which comprises more than one monomer. See definitions above. Since an oligonucleotide does not include within its definition an infinite number of nucleotides, this reading is untenable. Phrases of a claim cannot be read in isolation. Rather, all words of a claim must be given due weight.

Withdrawal of this rejection is requested in view of the amendments and comments provided.

Double Patenting

Claims 14-15, 18-21 and 42 are rejected as obvious over claims 1-22 of U.S. Patent 5,955,263. This rejection is respectfully traversed. The Patent and Trademark Office has previously held the two claim sets to be patentably distinct, and the Patent and Trademark Office is thus precluded by law (35 U.S.C. § 121) from making such a double patenting rejection. "A patent issuing on an application with respect to which a requirement for restriction has been made, or on an application filed as a result of such a requirement, shall not be used as a reference either in the Patent and Trademark Office or in the courts against a divisional application or against the original application or any patent issued on either one of them, if the divisional application is filed before the issuance of the patent on the other application." Application Serial Nos. 08/299,074 and 07/860,758 presented both original claims 1-13, 28-30, and original claims 14-21. In Restriction Requirements dated September 26, 1996, and April 6, 1993, the Patent and Trademark Office held these claims to be separately patentable. Copies enclosed. Applicants relied on the Patent and Trademark Office's

determination in filing the subject divisional patent application. Thus, the Patent and Trademark Office cannot now hold these sets of claims patentably indistinct and reject them for claiming the same invention.

Withdrawal of this invention is respectfully requested. A speedy notice of allowance is requested.

Respectfully submitted,

Date: November 8, 2002

By: Sarah A. Kagan

Sarah A. Kagan
Registration No. 32,141

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Customer No. 22907

Appendix – showing amendments in marked-up version

Specification

Substitute paragraph 1 on page 1 of the Preliminary Amendment with the following:

This is a divisional application of U.S. Serial No. 09/399,773, filed September 21, 1999, now U.S. Patent No. 6,245,515, which is a divisional application of U.S. Serial No. 08/299,074, filed September 1, 1994, now U.S. Patent No. 5,955,263 which is a divisional of U.S. Serial No. 07/860,758, filed March 31, 1992, now U.S. Patent No. 5,362,623, which is a Continuation-in-Part of U.S. Serial No. 07/715,182, filed June 14, 1991, now abandoned.

Claims

14. (Amended) A method of providing the physiological effect of wild-type p53 protein to a cell, comprising the step[s] of:

providing to a cell a compound which is [is] able to complex specifically with a p53-specific binding site, whereby the physiological effect of wild-type p53 protein is provided.

18. (Amended) The method of claim 15 wherein the oligonucleotide or oligonucleotide containing nucleotide analogs comprises the monomer sequence RRRCWWGYYY or the complement thereof.

19. (Amended) The method of claim 14 wherein the compound comprises an oligonucleotide or oligonucleotide containing nucleotide analogs wherein said oligonucleotide or oligonucleotide containing nucleotide analogs comprises at least one [a portion of the] monomer sequence RRRCWWGYYY as well as sequences adjacent to said monomer sequence in the human genome.

39. Cancel.

Amino Acids:

There are 20 naturally occuring amino acids that make up proteins. The basic chemical structural units of proteins are amino acids. With the exception of proline, amino acids have a common structure. The structure consists of a central carbon atom (the alpha carbon), to which is bonded to a amino acid (-NH2), a carboxyl group (-COOH), and a hydrogen atom. Amino acids in solution at isoelectric pH are mainly dipolar ions. This is generally how amino acids exist at cellular pH. The amino group (-NH2) accepts a proton and becomes (-NH3+), and the carboxyl group (-COOH) donates a proton and becomes dissociated (-COO-). Because of their amino and carboxyl groups, proteins in solution resist changes in acidity and alkalinity and so are important biological buffers.

- Amino acid definition

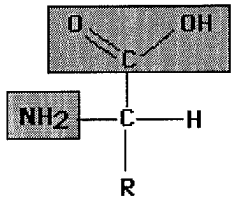

Fig. General formula for an amino acid molecule. "R" represents the variable groups that are attached to this basic molecule to make up the 20 common amino acids

---

The 20 amino acids are classified into subgroups, based on whether the R group is acidic, basic, neutral-polar, or neutral-nonpolar. Bound to the central carbon atom, each amino acid has an additional chemical group, called the R group. The R group varies from one amino acid to another; and, also gives each amino acid its distinctive properties. It is the organization of the R-group that gives a protein its structural and functional properties.

Amino acids with nonpolar R groups(also known as side chains) are classified as hydrophobic, whereas, those with polar side chains are classified as hydrophilic. Acidic amino acids have side chains that contain a carboxyl group. At cellular pH the carboxyl group is dissociated so that the R group has a negative charge. Basic amino acids are positively charged as a result of the dissociation of the amino group in their side chains. Acidic and basic chains ar ionic and therefore hydrophobic.

- Hydrophilic definition

- Hydrophobic definition

Amino acids are linked together by peptide bonds to form one or more macromolecule subunits called polypeptides. Long chains of polypeptides result in the formation of proteins. The primary animo acid sequence of a protein determines its secondary, tertiary, and quaternary structure, which then determines its functional state.

- Peptide bonds definition

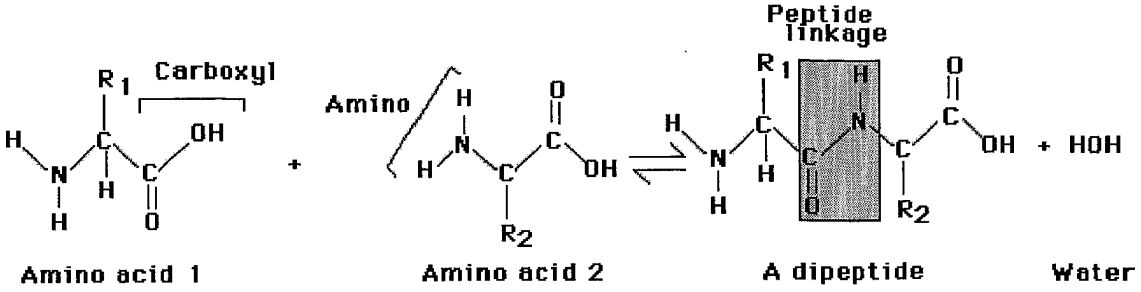

Fig. Formation of a peptide bond between two amino acids.

- Polypeptide definition

Because the alpha carbon of an amino acid is an asymmetric carbon, each amino acid can exist as two enantiomers. The two mirror images are called the L-isomer and the D-isomer. The amino acids present in living systems are almost exclusively L-isomers. The exceptions are a few D-amino acids present in the antibiotics produced by fungie.

- Enantiomer definition

In addition to the 20 common amino acids, some proteins have unusual amino acids. These rare amino acids are produced by the modification of common ones after they have become part of a protein.

With some exceptions, bacteria nad plants can synthesize all of their needed amino acids from simpler substances. If the proper raw materials are availiable, the cells of humans and animals can manufacture some, but not all, of the biologically significant amino acids. Those that humans and animals cannot synthesize, must be obtained through their diet, known as essential amino acids.

- Essential amino acids definition

Disulfide Amino Acid

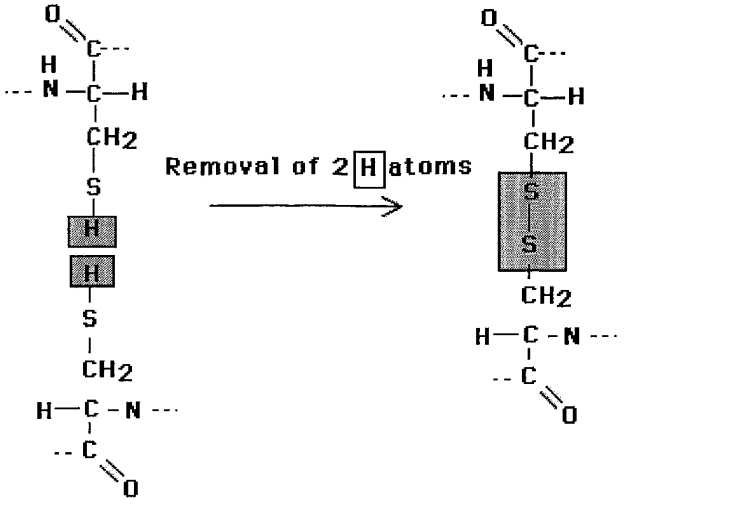

Fig. Formation of a disulfide bond (—S—S).

GLOSSARY

Amino acid: an organic compound containing an amino group (-NH2) and a carboxyl group (-COOH).

Enantiomers: are isomers (compounds that have the same molecular formula but different structures) that are mirror images of each other. Enantiomers may be designated D or L, depending on their configuration.

Essential amino acids: those amino acids that cannot be synthesized by the organism and must be obtained in the diet.

Hydrophilic: attracted to water.

Hydrophobic: repelled by water.

Peptide: a compound consisting of a chain of amino acid groups. A dipeptide consists of two amino acids, a polypeptide of many.

Peptide bonds: a distinctive covalent carbon-to-nitrogen bond that links amino acids in peptides and proteins.

Polypeptide: many amino acids bonded together.

REFERENCES

Berge Linda, Diane Martin, Eldra Solomon, and Claude Villee.1993. *Biology.* Third Edition. New York: Saunders College Publishing.

Russell, Peter J. 1996. *Genetics.* Fourth Edition. New York: Harper Collins College Publishers.

Return

Arts & Sciences | Biology | University | Graduate School
Perez Home | Natural Toxins Center | Classnotes

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Mueller: Emery's Elements of Medical Genetics

Contents

Glossary

Terms beginning with **O** from Emery's Elements of Medical Genetics:

Obligate carrier.
get definition

Oligogene.
get definition

Oligonucleotide.
get definition

A chain of, literally, a few nucleotides.

Oncogene.
get definition

Oncogenic.
get definition

Opsonization.
get definition

Polymerase chain reaction (PCR).
get definition

Polymorphic information content (PIC).
get definition

Polymorphism.
get definition

Polypeptide.
get definition

An organic compound consisting of three or more amino acids.

Polyploid.
get definition

Polyribosome.
get definition

Polysome (=polyribosome).
get definition

Population genetics.
get definition

DHH/SDK

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
08/299,074	09/01/94	VOGELSTEIN B	01107.47071

RECEIVED
18M170926
SEP 27 1996
BANNER & WITCOFF, LTD.

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WASHINGTON DC 20001-4597

EXAMINER	
EYLER, Y	
ART UNIT	PAPER NUMBER
1806	

DATE MAILED: 09/26/96

OIPE
NOV 08 2002
PATENT & TRADEMARK OFFICE
JC98

Please find below a communication from the EXAMINER in charge of this application.

Commissioner of Patents

RECEIVED
NOV 12 2002
TECH CENTER 1600/2900

47071 HOPK
DOCKETED
OCT 1 1996
Limited Restriction
Resp due 10/24/96
last day (2/27/97) 3 mo

PTOL-90 (Rev. 6/84)

2 - APPLICANT'S COPY

Office Action Summary

Application No.	Applicant(s)
08/299,074	Vogelstein et al
Examiner	**Group Art Unit**
Yvonne Eyler	1806

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire [redacted] thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-46* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☐ Claim(s) _____ is/are rejected.

☐ Claim(s) _____ is/are objected to.

☒ Claims *1-46* are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

✓ I. Claims 1-13, 43, and 44, drawn to a method of detecting p53, classified in class 435, subclass 7.1.

II. Claims 14-21 and 46, drawn to a method of providing the physiological effect of wild-type p53 to a cell, classified in class 514, subclass 44.

III. Claims 22 and 42, drawn to a double stranded DNA fragment containing a p53 binding site, classified in class 536, subclass 24.1.

IV. Claims 23-27 and 45, drawn to a single stranded oligonucleotide which binds to p53 specific binding sites, classified in class 536, subclass 25.3.

✓ V. Claims 28-30, drawn to a method of screening for compounds which bind to a p53-specific DNA binding sequence, classified in class 435, subclass 7.1.

VI. Claims 31-34, drawn to a method of genetic therapy providing a wild-type p53 gene to a cell, classified in class 514, subclass 44.

2. The inventions are distinct, each from the other because of the following reasons:

The method of Group I is entirely different from the method of Group II, having different method steps, using different compositions and having different expected outcomes. The method of Group I is designed to detect the presence of wild-type p53 protein in fluid and tissue samples. It does not provide any therapeutic or replacement benefit to the cell. The method of Group II is designed to replace lost p53 function but provides no mechanism to detect the actual presence or absence of p53. Likewise, the method of Group I is entirely different from that of Group VI. The

method of group VI is a gene therapy method designed to replace the p53 encoding sequence in a cell and thus restore function. The method of Group VI is not designed to detect p53 product nor is the method of Group I able to replace a gene.

The method of Group I is entirely different from the method of Group V, having different method steps, using different compositions and having different expected outcomes. The method of Group I is designed to detect the presence or absence of wild-type p53 through its ability to bind to specific DNA sequences. The method is not designed to detect any other compounds in the fluid or tissue sample which may also be able to bind to the DNA sequence used. The method of Group V, however, is designed to identify other compounds which will bind to a p53 specific DNA binding sequence and which will, in fact, compete with p53 for this sequence. It is not designed to detect the presence or absence of p53 in samples, but rather to screen compounds for binding ability.

The methods of Groups II and VI also are drawn to entirely different methods with different method steps, different compositions and different expected outcomes. The method of Group II is a treatment which is designed to provide a missing function through supplying a compound which is able to mimic or duplicate that function which is binding to a p53-specific binding site. The method does not provide reagents or steps to allow the replacement of the p53 gene. The method of Group VI provides steps for the replacement of the p53 gene but does not offer the treatments with compounds which bind to p53 specific DNA binding sites.

The inventions of Groups III, I and V are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, the product which consists of double stranded DNA sequence containing a p53 specific binding site may be used in multiple methods such as detecting wild-type p53 proteins, detecting p53 mutants which cannot bind, detecting other compounds capable of binding the sequence, or as a template for PCR.

Likewise, the inventions of Groups IV and II are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case, both may be shown. The method of Group II may be used with compounds other than the single stranded oligonucleotide of Group IV, such as polypeptides. The single stranded oligonucleotide of Group IV may be used in the method of Group II or as a probe in hybridization studies to identify other DNA fragments containing p53 specific binding sequences for example.

The compositions of Groups III and IV are not used (and are therefore independent of) in the method of Group V which utilizes the p53 gene.

Finally, the compositions of Groups III and IV are completely different, possessing different characteristics such binding specificity and strandedness. The compositions also have completely different utilities as detailed supra.

3. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classifications and their recognized divergent subject matter as well as the need for separate searches, restriction for examination purposes as indicated is proper.

4. A telephone call was made to Sarah A. Kagan on 08/27/96 to request an oral election to the above restriction requirement, but did not result in an election being made.

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yvonne Eyler, Ph.D. whose telephone number is (703) 308-6564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Yvonne Eyler, Ph.D.
September 23, 1996

Toni R. Scheiner

TONI R. SCHEINER
PRIMARY EXAMINER
GROUP 1800

APR 0 8 1993

UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

Address : COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
07/860,758	03/31/92	VOGELSTEIN	B 1107.038652

EXAMINER
SCHEINER, L.

BANNER, BIRCH, MCKIE & BECKETT
1001 G ST., N.W., 11TH FL
WASHINGTON, DC 20001-4597

1SM1

ART UNIT	PAPER NUMBER
1812	8

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

APR 0 8 1993

DATE MAILED: 04/06/93

AMEND DUE MAY 6, 1993

SAIC

☐ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire _____ month(s), 30 days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☑ Claims 1 - 41 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☐ Claims _____ are rejected.

5. ☐ Claims _____ are objected to.

6. ☑ Claims 1 - 41 are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).

12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____

13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

Restriction to one of the following inventions is required under 35 U.S.C. § 121:

I. Claims 1-13, 28-30 and 39, drawn to a method for detecting p53, classified in Class 435, subclass 5.

II. Claims 14-21, drawn to a method of providing a physiological effect to a cell, classified in Class 424, subclass 89.

III. Claims 31-34, drawn to a method of supplying wild-type p53 gene function, classified in Class 424, subclass 570.

IV. Claims 35-38, 40 and 41, drawn to a method of pre-screening agents for use in cancer therapy, classified in Class 436, subclass 64.

V. Claims 22-27, drawn to oligonucleotide compositions, classified in Class 435, subclass 6.

The inventions are distinct, each from the other because of the following reasons:

Inventions V and (I, II, III and IV) are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (M.P.E.P. § 806.05(h)). In the instant case the product as claimed can be used in a materially different process of using that product such as evidenced by the multiple processes claimed,

i.e. in detecting, providing a physiological effect, supplying gene function, and pre-screening agents for use in cancer therapy. Therefore, Inventions V and (I, II, III and IV) are novel and unobvious over each other and are patentably distinct inventions.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 C.F.R. § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 C.F.R. § 1.48(b) and by the fee required under 37 C.F.R. § 1.17(h).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laurie Scheiner whose telephone number is (703) 308-1122.

Papers related to this application may be submitted to Group 180 by facsimile transmission. Papers should be faxed to Group 180 via the PTO Fax Center located in Crystal Mall 1. The faxing

of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM 1 Fax Center number is (703) 308-4227.

LAS

Laurie Scheiner/LAS
April 5, 1993

ROBERT J. HILL, JR.
SUPERVISORY PATENT EXAMINER
GROUP 1800